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Polychlorinated biphenyls contamination in women with breast cancer

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Abstract

Background: Polychlorinated biphenyls (PCBs) are widespread highly resistant pollutants in the environment with potential adverse health effects on humans. The aim of the study was to compare PCBs contamination in women suffering from breast cancer with presumably healthy women. *Methods*: A gas-chromatography/mass-spectrometry method was used to identify and quantify seven PCBs congeners (IUPAC 28, 52, 101, 118, 138, 153,180) in blood from 60 cases of breast cancer and 60 age-matched healthy controls. *Results*: Cases and controls had similar risk profiles, except for menopausal status (respectively 82% vs. 65%, $p=0.014$). PCBs were detectable in 69.1% of the samples. Total blood level of PCBs was significantly different ($p=0.012$) in cases (7.08 ± 7.51 ppb) and controls (5.10 ± 5.15 ppb). The relationship between PCBs concentrations in serum and risk factor was mainly due to serum levels of PCB153, which were significantly higher in breast cancer women than in disease-free subjects (1.63 ± 1.26 ppb vs. 0.63 ± 0.78 ppb, $p<0.0001$), even after accounting for other potential risk factors. *Conclusions*: These results suggest that environmental exposure to PCBs may contribute to multifactorial pathogenesis of breast cancer.

Keywords: Breast cancer; Endocrine disrupters; PCBs

1. Introduction

Polychlorinated biphenyls (PCBs) are complex chemical mixtures that comprise theoretically 209 congeners, some of which are known to cause a wide range of adverse effects on animals and humans [1,2]. PCBs are industrial chemicals that have been used for diverse commercial applications such as hydraulic fluids, printing inks, or dielectric fluids for capacitors. The production and use of these compounds were banned in the late 1970s. Together with organochlorine pesticides, PCBs constitute what is called Persistent Organic Pollutants (POPs), due to their great chemical stability, their lipid solubility, and their ubiquitous prevalence in environment [3,4]. Adults are mainly exposed through the consumption of dairy products, meat and fish. The presence of POPs in human serum and adipose tissue has been reported in many studies over the last three decades. Several

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test, Institut National Santé Publique, Québec) was performed as external quality control.

2.3. Statistical analysis

Serum levels of PCBs were expressed as mean ± SD. Correction for lipid content was tested, but since the results were not affected, only crude data are presented. Quantitative continuous results were not categorized but a log-transform was applied to PCBs data to normalize their distributions. All subsequent statistical analyses were carried out on the transformed data. Risk factors and PCBs serum levels in cases and controls were compared by means of ordinary logistic regression, not only for each congener separately but also for all PCBs simultaneously. In every comparison, age was included in the analysis. Results were expressed as odds ratios (OR) and associated 95% confidence intervals (CI). In the multivariate analysis, adjustment was made for potential confounding risk factors: menopausal status, number of full-term pregnancies, lactation, use of HRT and family history of breast cancer. Results were confirmed after backward elimination of not significant effects. All results were considered to be significant at the 5% critical level ($p<0.05$). Calculations were done using the SAS (SAS Institute, version 8.2 for Windows) and S-Plus (version 6.2) statistical packages.

3. Results and discussion

3.1. Risk factors

The characteristics of cases and controls are displayed in Table 1. The two groups had similar risk profiles but the prevalence of menopause was significantly higher in women with breast cancer, yielding to an odds ratio of 3.8 (95% CI: 1.3–11).

3.2. PCB concentrations

PCBs 28 and 118 could not be detected in any of the subjects of the study. The distributions of the five other congeners in cases and controls are presented in Table 2. For PCBs 52, 101 and 180, serum concentrations did not differ in the two groups. By contrast, the serum concentrations of PCB138 and PCB153 were significantly higher in cases than in controls. The same observation was made for total PCB content ($p=0.012$).

Table 1
Characteristics of risk factors in women with breast cancer (cases) and in disease-free women (controls) of similar age

	Cases ($n=60$)	Controls ($n=60$)	p^a
Age of menarche, mean years (SD)	11.4 (0.95)	11.5 (1.08)	0.59
Menopause, n (%)	49 (81.7)	39 (65.0)	0.014
HRT[b], n (%)	30 (61.2)	26 (66.7)	0.45
Parity, n (%)	34 (56.7)	33 (55.0)	0.85
Breast feeding[c], n (%)	24 (70.6)	25 (75.6)	0.85
Family history of breast cancer, n (%)	9 (15.0)	5 (8.30)	0.25

[a] p-value adjusted for age.
[b] Restricted to menopaused women.
[c] Restricted to parous women.

3.3. Association with breast cancer

All PCB concentrations and confounding risk factors for breast cancer were combined into a multiple logistic regression analysis (see Table 3). It is seen that menopause ($p=0.038$) and PCB153 ($p<0.0001$) remained statistically discriminate between cases and controls while the effect of PCB138 disappeared. Thus, high concentrations of PCB153 are significantly associated with an increased risk of breast cancer despite the presence of other factors, menopause in particular. After backward elimination of not significant effects, menopause and serum PCB 153 concentration remained significant (respectively, $p=0{,}036$ and $p<0{,}0001$), reinforcing the previous conclusion. Similar results were obtained when replacing individual PCBs by total PCB content. The only two significant variables were menopausal status ($p=0.015$) and total serum PCB concentration ($p=0.035$).

3.4. Discussion

In the present case-control study, PCB153, as already suggested by a previous limited study [21] and, to a lesser extent, PCB138 were found in significantly higher concentration in blood samples of women diagnosed with breast cancer when compared to a control group of disease free subjects of the same age. In our study, serum PCB153 concentration

References

[1] Brouwer A, Longnecker MP, Birnbaum LS, Cogliano J, Kostyniak P, Moore J, et al. Characterization of potential endocrine-related heath effects at low dose levels of exposure to PCBs. Environ Health Perspect 1999;107(Suppl. 4):639–49.

[2] Mc Kinney JD, Waller CL. PCBs as hormonally active structural analogues. Environ Health Perspect 1994;102:290–7.

[3] Chevreuil M, Granier L. Les PCBs, des polluants difficiles à éliminer La recherche 1992;23:484–6.

[4] Safe SH. PCBs: environmental impact, biochemical and toxic responses and implications for risk assessment. Crit Rev Toxicol 1994;24:87–149.

[5] Korach KS, Sarver P, Chae K, Mc Lachlan JA, Mc Kinney JD. Estrogen receptor binding activity of polychlorinated hydroxy-biphenyls: conformationally restricted structural probes. Mol Pharmacol 1988;33:120–6.

[6] Robinson AK, Sirbasku DA, Stancel GM. DDT supports the growth of an estrogen-responsive tumour. Toxicol Lett 1985;27:109–13.

[7] Connor K, Ramamoorthy K, Moore M, Mustain M, Chen I, Safe S, et al Hydroxylated PCBs as estrogens and antiestrogens. structure–activity relationship. Toxicol Appl Pharmacol 1997;142:160–8.

[8] Gellert JR. Uterotrophic activity of PCBs and induction of precocious reproductive ageing in neonatally treated female rats. Environ Res 1978;16:123–30.

[9] Jansen HT, Cookes PS, Porcelli J, Liu T-C, Hansen LG. Estrogenic and antiestrogenic actions of PCBs in female rats: in vitro and in vivo studies. Reprod Toxicol 1993;7. 237–48.

[10] Oliva A, Spira A, Multigner L. Contribution of environmental factors to the risk of male infertility. Hum Reprod 2001;16: 1768–76.

[11] Giwercan AE, Skakkebaek NE. The human testis: an organ at risk? Int J Androl 1992;15:373–85.

[12] Shain W, Bush B, Seegal R. Neurotoxicity of PCBs: structure–activity relationship of individual congeners. Toxicol Appl Pharmacol 1991;111:33–42.

[13] Cocco P. On the rumors about the silent spring. Review of the scientific evidence linking the occupational and environmental pesticide exposure to endocrine disruption health effects. Cad Saùde Pùblica 2002;18:379–402.

[14] Laden F, Hankinson SE, Wolff MS, Colditz GA, Willett WC, Speizer FE, et al. Plasma organochlorine levels and the risk of breast cancer: an extended follow-up in the nurse's health study. Int J Cancer 2001;91:568–74.

[15] Aronson KJ, Miller AB, Woolcott CG, Sterns EE, McGready DR, Lickley LA, et al. Breast adipose tissue concentrations of polychlorinated biphenyls and other organochlorines and breast cancer risk. Cancer Epidemiol Biomarkers Prev 2000;9:55–63.

[16] Davis DL, Bradlow HL, Wolff M, Woodruff T, Hoel DG, Anton-Culver H. Medical hypothesis: xenoestrogens as preventable causes of breast cancer. Environ Health Perspect 1993;101:372–7.

[17] Hoyer AP, Grandjean P, Jorgensen T, Brock JW, Hartvig HB. Organochlorine exposure and risk of breast cancer. Lancet 1998;352.1816–20.

[18] Moysich KB, Ambrosone CB, Vena JE, Shields PG, Mendola P, Kostyniak P, et al Environmental organochlorine exposure and postmenopausal breast cancer risk. Cancer Epidemiol Biomarkers Prev 1998;7:181–8.

[19] Charlier C, Albert A, Herman P, Hamoir E, Gaspard U, Meurisse M, et al. Breast cancer and serum level of organochlorines residues. Occup Environ Med 2003;60:348–51.

[20] Charlier C, Dubois N, Cucchiaro S, Plomteux G. Analysis of PCBs in human plasma by GC-MS. J Anal Toxicol 2003;27: 42–5

[21] Charlier C, Pitance F, Plomteux G. PCBs residues in a breast cancer population. Bull Environ Contam Toxicol 2003;71: 887–91.

[22] Pauwels A, Covaci A, Weyler J, Delbeke L, Dhont M, De Sutter P, et al. Comparison of POP residues in serum and adipose tissue in a female population in Belgium, 1996–1998. Arch Environ Contam Toxicol 2000;39:267–70.

[23] Gladen BC, Doucet J, Hansen LG Assessing human PCBs contamination for epidemiologic studies: lessons from patterns of congener concentrations in candians in 1992. Environ Health Perspect 2003;111:437–43.

[24] Wolff MS, Toniolo PG. Environmental organochlorine exposure as a potential etiologic factor in breast cancer. Environ Health Perspect 1995;103(Suppl. 7):141–5.

[25] Wolff MS, Camann D, Gammon M. Proposed PCB congener grouping for epidemiologic studies. Environ Health Perspect 1997;105:13–4.

[26] Oakley GG, Devanaboyina US, Robertson LW. Oxidative DNA damage induced by activation of polychlorinated biphenyls (PCBs): implications for PCB-induced oxidative stress in breast cancer. Chem Res Toxicol 1996;9:1285–92.

[27] Bucholski KA, Begerov J, Winneke G, Dunemann L. Determination of PCBs and chlorinated pesticides in human body fluids and tissues. J Chromatogr A 1996;754:479–85

[28] Holford TR, Zheng T, Maynet ST, Zahm SH, Tessari JD, Boyle P. Joint effects of nine PCBs congeners on breast cancer risk. Int J Epidemiol 2000;29:975–82.

[29] Garrido-Frenich A, Martinez Vidal JL, Moreno Frias M, Olea Serrano F, Olea N. Quantitative determination of endocrine-disrupting PCBs and organochlorinated pesticides in human serum using GC with ECD and tandem MS. J Mass Spectrom 2000;35:967–75.

[30] Lucena RA, Allam MF, Costabeber IH, Villarejo ML, Navajas RF. Breast cancer risk factors: PCBs congeners. Eur J Cancer Prev 2001;10·117–9.

[31] Zheng T, Holford TR, Tessari J, Mayne ST, Owens PH, Ward B, et al. Breast cancer risk associated with congeners of PCBs. Am J Epidemiol 2000;152.50–8.

[32] Millikan R, De Voto E, Duell EJ, Tse CK, Savitz DA, Beach J, et al. DDE, PCBs and breast cancer among African-American and white women in North Carolina. Cancer Epidemiol Biomarkers Prev 2000;9:1233–40.